Rhythm is the basis of life. Physiology explores the dynamic equilibrium of our bodies as we interact with the rhythms of our surrounding environment. This interaction is essential for our wellness. In Physiology, we publish review articles that explore a wide range of themes. In this issue, we introduce two of these themes: Rhythms of Life and Striving for Wellness.

**Rhythms of Life**

Previous issues of Physiology have explored all aspects of the rhythms of life that can be categorized by their relationship to our 24-h cycle: circadian, ultradian, and infradian (4). Ultradian rhythms take a variety of forms from the repetitive beating of our hearts (8) to the respiratory rhythm to feeding behavior and metabolism (3). Infradian rhythms include cycles associated with reproduction, seasonal change, and aging.

It is not surprising that the major environmental stimulus is a 24-h pattern of light and dark that represents a clock that entrains various aspects of our physiology. It is important to note that circadian means “around,” such that if our days become longer or shorter, physiological rhythms are affected. The concept of zeitgeber (“time giver”) has been a central part of physiology since the beginnings of the scientific discipline. The strongest zeitgeber is light itself, which can entrain physiological processes even with limited light exposure. Unless we live at equatorial regions, periods of light and dark vary with the seasons. Thus the timing of the light signal gradually shifts and our bodies adjust to this shifting pattern via the zeitgeber signal. In the most northern and southern regions of Earth, the duration of daylight can be dramatically altered even to the extent of constant darkness. Some individuals have considerable difficulty in adjusting their physiology to these conditions. Exposure to artificial light, if timed properly, can help. For example, seasonal affective disorders including depressive symptoms can be ameliorated by short-term exposure to artificial light early in the day. World travelers experience the impact of abrupt changes in the timing of their exposure to light as they cross time zones and become jet lagged. Shift workers undergo a similar jet lag experience without travel. One commercial treatment for jet lag is light therapy that is timed based on the time shift to the new environment. The pineal gland is sensitive to light and excretes melatonin, which may serve as the underlying physiological basis for the light zeitgeber. Indeed, melatonin treatment is also used to mitigate jet lag.

The neural circadian clock has been located in the hypothalamic suprachiasmatic nucleus (SCN). Projections from the SCN influence a number of motor, sensory, and autonomic systems. Thus we have circadian gradations in neural (2) and locomotor patterns (7), reflex excitability, sensory thresholds, body temperature, blood pressure regulation, and respiratory patterns—almost everything influenced by the central nervous system (CNS). But we do not rely on just one master clock region. It now appears that every cell expresses a “clock” gene and that circadian rhythms can be observed even at the cellular level. Obviously, there is much more to be learned about the physiology of circadian rhythms.

Throughout evolution, animals exploited the external circadian patterns of daylight and nighttime to feed or avoid being food. Hence, the cycles of both predators and prey assumed either a diurnal or nocturnal pattern where activity was limited to essentially half the day and rest consumed the remainder. Not surprisingly, metabolic patterns also follow a circadian rhythm. However, within the limited periods of activity and inactivity, shorter duration rhythms also emerged in feeding patterns and metabolism. We all experience these ultradian cycles in our digestive systems as we distribute our meals throughout the day. Ultradian cycles are still linked to circadian rhythms such that disruptions in one will lead to disruptions in the other.

Additional ultradian rhythms are driven by the CNS and are not as directly affected by the circadian clock. We seldom think about our rhythmic pattern of breathing as it continues throughout the day. Recent studies have suggested that the central pattern generator for breathing in mammals is located in the pre-Bötzinger complex of the brain stem. The basic pattern of breathing remains the same, although it is affected by the circadian patterns of activity and rest as metabolic demands change. Other central pattern generators exist for rhythmic motor behaviors such as mastication, walking, or running. In every case, although the motor pattern may appear relatively simple, the central pattern generators for these rhythms are highly organized and complex, involving coordinated neural activation of multiple muscles.

Other rhythmic patterns are generated outside the CNS, the most obvious being the cardiac rhythm. These patterns are typically generated by pacemaker cells with complex interaction between conductances for various ions that affect membrane excitability and action potential generation. In addition to the heart, there are rhythmic contractions of muscles controlling gastrointestinal motility and uterine contractions. Indeed, barring intervention, most of us came into this world as a result of ultradian rhythmic contractions of our mother’s womb. Thus it is hard to argue the importance of ultradian rhythms.

A regularly occurring physiological process that recurs at longer than 24 h is infradian. In mice and rats, the reproductive cycle is 2–5 days, in humans 28 days, and in elephants nearly 6 months. These infradian rhythms are also influenced by the circadian clock as well as other factors related to environmental exposure. Seasonal cycles entrain many infradian rhythms coordinating the timing of births across many species. It is obvious that to be healthy and productive we depend on the “rhythms of life.” It is the basis of our wellness.

**Striving for Wellness**

Control of communicable diseases is a crucial step in creating the modern vision of a productive society. Physiology research plays an integral part in advancing our understanding of disease processes and treatments resulting from this knowledge have successfully reduced mortality and extended human life expectancy (5). Currently, in most developed nations...
where lifestyle-related “diseases” are approaching pandemic levels, striving for wellness and preserving the effort that helped to increase life expectancy is key to retaining a productive society. The Merriam-Webster definition of wellness is the state of being in good health as an actively sought goal, but understanding how to achieve wellness is still a challenge. Avoiding disease and striving for wellness can be seen as opposite sides of the same theoretical coin; we need to understand the causes of disease to prevent them, but we also need to understand how to optimize physiological performance to improve and sustain a high quality of life and limit the disability that comes with largely preventable, chronic diseases.

Primary aging physiology, or aging resulting from innate maturational processes independent of pathological or environmental causes, explains how organisms function throughout the life span. Many of the common conditions associated with aging humans are considered secondary aging. In this context, Frank Booth and colleagues have described physical inactivity and sedentary behaviors as major causes of secondary aging and propose that physical inactivity contributes to earlier onset of chronic disease, frailty, and lower quality of life (1). In addition to reducing an individual’s overall wellness profile, it is now known from inactivity physiology research that even short periods of inactivity (days or weeks) can temporarily reduce insulin sensitivity and cause endothelial dysfunction in healthy humans. Recently, “healthy” octogenarians with a sedentary lifestyle were compared to age-matched life-long athletes (10). Both groups were healthy by clinical standards and lived independently. However, the octogenarian athletes had higher cardiopulmonary capacity and mitochondrial oxidative capacity, providing a larger functional reserve to both engage in a wide variety of challenging activities and also delay the onset of disability. This suggests that there is a substantial physiological “cost” of something as common as not exercising regularly.

In contrast to sedentary behaviors, habitual physical activity is associated with a lower risk of mortality from cardiometabolic disease. Exercise training improves the function of endothelial cells in active skeletal muscle vascular beds, yet the beneficial effects extend to the systemic circulation. Laughlin and colleagues have reviewed such vascular and circulatory adaptations to chronic exercise (9). Maintaining the vascular system’s ability to adequately perfuse organs is essential to support optimal function of the heart, brain, kidneys, and other organs throughout the life span. Emerging evidence suggests that the maintenance of plasticity of the vascular system may also explain the favorable effect of physical activity on cognitive function and lower incidence of dementia.

Even in the absence of chronic disease, it is clear that regular exercise is a necessary wellness component to optimize physical function. Although habitual exercise improves traditional disease risk factors, this measurable effect does not fully account for the reduction in morbidity and mortality associated with increasing levels of physical activity (6). Furthermore, exercise is far more protective than the medical community can currently appreciate. Understanding the physiological effects of physical inactivity, habitual exercise, and other lifestyle behaviors will not only promote wellness but also may identify future biomarkers of functional ability or disease.

References